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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,627	04/28/2006	Derek Nigel John Hart	DAVI257.004APC	9936

20995 7590 12/23/2008

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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
12/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/577,627	HART ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-33 and 37* is/are pending in the application.

4a) Of the above claim(s) *25-28,30 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24,29,31,32 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-7-07 8-29-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election and amendment filed September 22, 2008 is acknowledged.

   Claims 1-20 and 34-36 have been canceled.

   Claims 21-33 and 37 are pending.

2. Applicant's election of Group VI, drawn to a method for assessing the immunological potential of a subject said method comprising obtaining a sample from said subject comprising T-cells and subjecting the sample to cell surface discrimination means to determine the presence, absence or level of CD4+ CMRF-35++ CD45RO+ and CD4+ CMRF-35++ CD45RO+CXCR3+ T-cells, and the species of subject whose immunological potential will be assessed is "a subject having psoriasis," in the reply filed on September 22, 2008 is acknowledged.

   Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

   The restriction requirement put forth in the Office Action mailed May 20, 2008 is hereby made final.

   Claims 21-24, 29, 31, 32 and 37 are under examination as they read on a method for assessing the immunological potential of a subject said method comprising obtaining a sample from said subject comprising T-cells and subjecting the sample to cell surface discrimination means to determine the presence, absence or level of CD4+ CMRF-35++ CD45RO+ or CD4+ CMRF-35++ CD45RO+CXCR3+ T-cells, wherein the elected species of subject whose immunological potential will be assessed is "a subject having psoriasis."

   Moreover, claims 25-28, 30 and 33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species of invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 22, 2008.

3. The specification is objected to in that 35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." Many sections of the specification are not clear or exact. Appropriate correction is required.

   Here are some examples of unclear or inexact Sections of the specification:

- In the Brief Description of the Drawings the experiment upon which the data in Figure 2 is presumably based is disclosed. However, there does not appear to be any indication in the

Brief Description of the Drawings or the elsewhere in the specification as to which particular T-cell populations/assay conditions correspond to the bars shown in Figure 2.

Thus, it is not possible to accurately evaluate the meaning of the data displayed in Figure 2.

- In the Brief Description of the Drawings the experiment upon which the data in Figure 4 is presumably based is disclosed. However, there does not appear to be any indication in the Brief Description of the Drawings or the elsewhere in specification as to which particular T-cell populations/assay conditions correspond to the dot blots shown in Figure 4.

  Moreover, the detailed description of the invention discloses the following at page 98, 1st sentence (emphasis added): "The differences in the susceptibility of the CMRF-3+CD4+ T lymphocyte compared to CMRF-35-CD4+ T lymphocyte to undergo apoptosis was apparent by 4 hours ***when PMA/ ionomycin was used to activate the cells (Figure 4)***."

  However, the brief description of Figure 4 on page 8 of the specification describes the use of immobilized anti-CD3/CD28 antibodies to activate the cells not PMA/ ionomycin.

  Thus, it is not possible to accurately evaluate the meaning of the data displayed in Figure 4.

- The Detailed Description of the Invention discloses at page 98, under the heading "EXAMPLE 19", (emphasis added): "CMRF-35+ ***CD45RO***+ CXCR3+ T cells are depleted from the peripheral blood of patients with psoriasis".

  Immediately following this sentence, the specification discloses (emphasis added): "Using the above-identified methods, PBMCs were isolated from the peripheral blood of normal donors and patients with psoriasis, ***and the CD4+ T cells stained for CMRF-35 and CXCR3***. Analysis demonstrated that the CMRF-35++/CXCR3 population of cells is significantly reduced in the peripheral blood of patients with psoriasis, compared to normal controls (FIG. 6)."

  First, it would not be entirely clear to the skilled artisan what the phrase "Using the above-identified methods…" refers to as this is the 19th Example and there are many methods that precede it.

  However, even setting this aside, this disclosure is still not clear or exact in that while the heading for this example states "CMRF-35+ ***CD45RO***+ CXCR3+ T cells are depleted from the peripheral blood of patients with psoriasis" the body of the example does not mention staining for "CD45RO+," i.e., "PBMCs were isolated from the peripheral blood of normal donors and patients with psoriasis, and the CD4+ T cells stained for CMRF-35 and CXCR3."

  Furthermore, the only other references to Figure 6 which occurs in the brief description of the drawings also fails to mention CD45RO+ (emphasis added): "Figure 6 is a graphical representation of a dot blot analysis. PBMCs from a normal donor and a patient with

psoriasis were analyzed using flow cytometry. ***CD4+ T cells were stained for the expression of CXCR3 and CMFR-35***. Analysis revealed that patients with psoriasis had significantly ***reduced levels of CXCR3+ CMRF35++ CD4+ T cells***.

Thus, while nearly all of the disclosure surrounding Figure 6 seems to indicate that CD4+ CMRF35++ CXCR3+ were measured, it is still uncertain exactly what is being disclosed.

4. The specification makes reference to Figures xb, 2C and 3C which are not found in the Drawings (see instant specification pages 95-96). When a specification refers to Figures not present MPEP 601.01(g) instructs applicant is required to do one of the following:

   (A) accept the application, as filed, without all of the drawing figure(s) referred to in the specification;

   (B) file any omitted drawing figure(s) with an oath or declaration in compliance with 37 CFR 1.63 and 37 CFR 1.64 referring to the omitted drawing figure(s) and a petition under 37 CFR 1.182 with the petition fee set forth in 37 CFR 1.17(f), requesting the date of submission of the omitted drawing figure(s) as the application filing date; or

   (C) file a petition under 37 CFR 1.53(e) with the petition fee set forth in 37 CFR 1.17(f) alleging that the drawing figure(s) indicated as omitted was in fact deposited with the USPTO with the application papers, including any and all evidence supporting the allegation. See MPEP § 503. The petition fee will be refunded if it is determined that the drawing figure(s) was in fact received by the USPTO with the application papers deposited on filing.

   Further details as to how to appropriately meet the requirement of (A), (B) or (C) are provided in MPEP 601.01(g).

5. The disclosure is objected to because of the following informalities: on page 99, 1st paragraph, “Breast" is not a disease. Also “Thrombocyopenia”, "throiditis”, “Grave Disease” and “duseases” are misspelled. Appropriate correction is required.

   The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

   > The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 21-24, 29, 31, 32 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was

not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims recite (emphasis added), "a method for assessing the ***immunological potential*** of a subject said method comprising…" measuring the level of five subsets of CD4+ T cells, CMRF-35++CD45RO+; CMRF-35+CD45RO+; CMRF-35-CD45RO+; CMRF-35+CD45RO- and CMRF-35-CD45RO-.

The phrase "immunological potential" is not defined by the instant specification. This phrase, given its broadest reasonable interpretation consistent with the instant specification and its use by those of skill in the art, encompasses in its breadth anything that alters the ability of subject's immune system to respond to an antigen, be it an alloantigen or an autoantigen.

However, the instant specification fails to provide sufficient objective evidence or sound scientific reasoning to establish that an overabundance or a deficiency in any of these subsets, for example in the peripheral blood and/or the tissues and/or the lymphatic system, lead to a change in the "immunological potential" of a subject (see below).

The utility of the claimed invention cannot lie in merely measuring the level of various subsets of cells in a subject so as to carry out further research on how an overabundance or a deficiency in any of these subsets affects the health of the subject being tested.

Rather, the utility of the claimed method lies in measuring the level of various subsets of cells so as to assess the "immunological potential" of a subject as it relates to disease.

The prior art teaches CD45RO+CXCR3+ memory T cells are found in the psoriatic skin infiltrate and are further over-abundant in lymph node of a psoriatic animal model (see e.g., Hong et al., J Immunol. 2001 Apr 1;166(7):4765-72, in particular page 4769, left column, 1st and 2nd paragraphs and Gniadecki et al., Expert Opin Emerg Drugs. 2002 May;7(1):69-90, in particular column bridging paragraph on page 74). Furthermore, two single nucleotide polymorphisms found in CMRF-35 family genes are linked to psoriasis (see, e.g., Speckman et al., Hum Genet. 2003 Jan;112(1):34-41, in particular Abstract).

Thus, the level of CMRF-35++CD45RO+CXCR3+ T-cells in the peripheral blood or the tissues or the lymphatic system could potentially be indicative of the "immunological potential" of a psoriasis patient if one considers the claimed "immunological potential" to be the potential of CMRF-35++CD45RO+CXCR3+ T-cells to participate in inducing and/or maintaining the inflammatory immune response that promotes psoriasis.

However, while the skilled artisan would certainly consider this to be a plausible hypothesis, the instant specification fails to enable the skilled artisan to practice this embodiment of the claimed method, much less the full breadth of the claimed method, in the absence of further exploratory research and undue experimentation.

With respect to the distribution of CMRF-35 cells in psoriasis, the instant specification discloses at page 5, 1st paragraph, "[o]f the CD4+ sub-populations of T-cells, the CMRF-35++ CD45RO+ and more particularly, CMRF-35++ CD45RO+ CXCR3+ sub-populations are particularly important. For example, in psoriasis, these populations are absent from peripheral blood. This indicates a role of these sub-populations of T-cells in psoriasis and potentially other inflammatory conditions or conditions which provoke or which are exacerbated by an immunological response."

In contrast to the assertion of altered levels of peripheral blood CD4+CMRF-35++ CD45RO+ T cells in psoriasis patients, the instant specification further discloses at page 99, 1st paragraph that peripheral blood cells from breast [cancer?], Multiple myeloma, Non Hodgkin's lymphoma, Rheumatoid arthritis, Thyrotoxicosis, SLE, IgA Nephropathy, Idiopathic Thrombocyopenia Purpura, Hashimoto's throiditis, Coeliac Disease and Graves Disease were analyzed for CD4+CD45RO+CMRF-35++ and "[t]here was no similar change in the CD4+CD45RO++CMRF-35++ population in any of these [diseases] as seen for psoriasis."

Thus, applicant's disclosure asserts that the number of peripheral blood CD4+CMRF-35++ CD45RO+ and CD4+CMRF-35++ CD45RO+ CXCR3+ T-cells are decreased in psoriasis but not in a variety of other diseases including the inflammatory condition "rheumatoid arthritis" (see claim 33).

Consequently, the skilled artisan would not be able to practice the claimed method to assess the immunological potential of a subject having any one of Multiple myeloma, Non Hodgkin's lymphoma, Rheumatoid arthritis, Thyrotoxicosis, SLE, IgA Nephropathy, Idiopathic Thrombocytopenia Purpura, Hashimoto's thyroiditis, Coeliac Disease or Graves' Disease.

That said, even with respect to the assertedly decreased levels of peripheral blood CD4+CMRF-35++ CD45RO+ and CD4+CMRF-35++ CD45RO+ CXCR3+ T-cells in psoriasis, the skilled artisan would be hard pressed to say what this implies as to the "immunological potential" of a psoriasis patient.

On the one hand, the instant specification shows CD4+CMRF-35+ cells produce more IFN-γ than CD4+CMRF-35- cells both in response to T cell mitogens or CD3/CD28 and in a mixed lymphocyte reaction with HLA-DR+ Lin- dendritic cells as stimulators. Given that INF-γ production is a hallmark of psoriasis (see, e.g., Gniadecki, in particular page 73 right column, 1st-3rd paragraph), what do the asserted decreased levels of peripheral blood CD4+CMRF-35++ CD45RO+ and CD4+CMRF-35++ CD45RO+ CXCR3+ T-cells say about the "immunological potential" of a psoriasis patient? Put another way, what would the skilled artisan draw from this observation, i.e., does the psoriasis patient with fewer peripheral blood CD4+CMRF-35++ CD45RO+ or CD4+CMRF-35++ CD45RO+ CXCR3+ T-cells have greater or lesser "immunological potential" to respond to the psoriasis antigen(s)? Further

exploratory research and undue experimentation would be required to understand the significance of this observation as it relates to the "immunological potential" of the subject.

On the other hand, the prior art indicates CD45RO+CXCR3+ T-cells are found in the psoriatic skin infiltrate and are further over-abundant in lymph node of a psoriatic animal model (see e.g., Hong, in particular page 4769, left column, 1st and 2nd paragraphs and Gniadecki, in particular column bridging paragraph on page 74). Are the CD45RO+CXCR3+ T-cells found in the psoriatic skin infiltrate/over-abundant in lymph node of a psoriatic animal model also CMRF-35++ type cells, or do the assertedly decreased levels of peripheral blood CD4+CMRF-35++ CD45RO+ and CD4+CMRF-35++ CD45RO+ CXCR3+ T-cells arise as a consequence of apoptosis? (According to the instant specification paragraph bridging pages 97-98, these cells are prone to PMA/ionomycin or anti-CD3/CD28 activation induced apoptosis as compared to CD4+CMRF- T cells).

Again, what would the skilled artisan draw from this observation, i.e., does the psoriasis patient with fewer peripheral blood CD4+CMRF-35++ CD45RO+ or CD4+CMRF-35++ CD45RO+ CXCR3+ T-cells have greater or lesser "immunological potential" to respond to the psoriasis antigen(s)?

Furthermore, the degree to which the levels of CD4+CMRF++CD45RO+ T cells in particular are altered in psoriasis versus normal subjects is unpredictable and uncertain based on the disclosure of the instant specification.

As stated above, the instant specification discloses at page 5, 1st paragraph, "[o]f the CD4+ sub-populations of T-cells, the CMRF-35++ CD45RO+ and more particularly, CMRF-35++ CD45RO+ CXCR3+ sub-populations are particularly important. For example, in psoriasis, these populations are absent from peripheral blood. This indicates a role of these sub-populations of T-cells in psoriasis and potentially other inflammatory conditions or conditions which provoke or which are exacerbated by an immunological response."

However, on page 100 the specification shows a graphic portrays the level of binding of the CMRF-35 mAb measured as mean fluorescence intensity (MFI) wherein the cells being assessed appear to have been initially selected based on their CD4/CD45RO/CMRF-35 surface phenotype. For example, it appears that columns 1 and 7 of this graphic display the level of binding of the CMRF-35 mAb measured as MFI for the cells having the phenotype CD4+CD45RO+CMRF-35++ in psoriasis patients and normal subjects, respectively. From this graphic it appears that the average MFI in psoriasis patients is only marginally less than in normal subjects, see columns 1 vs. 7. Moreover, there is a very broad distribution of MFIs in both psoriasis patients and normal subjects indicating that the level of CMRF-35 MFI for any given individual is highly variable.

It is further noted the instant claims recite (emphasis added), "A method…comprising obtaining a sample from said subject comprising T-cells ***and subjecting the sample to cell***

surface discrimination means to determine the presence, absence or level of CD4+ T-cells selected from the list consisting of…"

While the claims do not recite "means for' or "step for" the phrase "subjecting the sample to cell surface discrimination means to determine the presence, absence or level of CD4+ T-cells" is sufficiently close so as to qualify as an invocation of 35 U.S.C. § 112, 6th paragraph. Moreover, the instant specification discloses corresponding structure and acts for discriminating cell surface expression levels of the T-cell markers CD4 and CD45RO.

However, the instant specification does not provide an enabling disclosure of a means for discriminating cell surface expression levels of "CMRF-35". There are several reasons that the instant specification is not enabling in this regard.

"CMRF-35" as its recited in the instant claims, i.e., "CMRF-35++" OR "CMRF-35+" OR "CMRF-35-", given its broadest reasonable interpretation consistent with the instant specification and with the use of this term in the art, encompasses a family of CMRF-35 molecules including CMRF-35A, CMRF-35A2, CMRF-35A3, CMRF-35A4, CMRF-35A6 and CMRF-35H (see instant specification page 2, 2nd and 3rd paragraphs and page 4, 3rd paragraph as well as Speckman, ibid).

The instant specification does not provide teachings as to the significance of the CMRF-35A2, CMRF-35A3, CMRF-35A4, CMRF-35A6 with respect to the "immunological potential of a subject". Moreover, the instant specification provides no direction or guidance with respect to the expression of the CMRF-35 family members other than CMRF-35A and CMRF-35H on CD4+CD45RO+ cells. Thus, the instant specification cannot be said to enable the claimed method wherein the CMRF-35 being measured is CMRF-35A2, CMRF-35A3, CMRF-35A4, CMRF-35A6. Furthermore, as to measuring CMRF-35A and CMRF-35H on CD4+CD45RO+ cells, the claimed method requires the skilled artisan to discriminate between CMRF-35-, CMRF-35+ and CMRF-35++ expression on the cell surface.

However, as is well know to one of skill in the immunology art, different antibodies raised against a common protein, such as CMRF-35A or CMRF-35H, will have a variety of antigen affinities and epitope specificities. Thus, it would not be a matter of routine experimentation for the skilled artisan to practice applicant's claimed method simply by making their own anti-CMRF-35A and anti-CMRF-35H antibody or antibodies, especially so without having applicant's CMRF-35 antibody and CMRF-35++/+/- cell lines as references for what the claimed "CMRF-35++" or "CMRF-35+" or "CMRF-35-" actually looks like.

Moreover, that the "CMRF-35" antibody used throughout the working examples instant specification binds an undisclosed epitope common to CMRF-35A and CMRF-35H (these molecules having 80% similarity in their extracellular Ig type domains) adds an additional layer of complexity to trying to replicate applicant's claimed invention without having access to the "CMRF-35" antibody.

As a required element, the "CMRF-35" antibody used throughout the working examples of the instant specification must be known and readily available to the public or obtainable by a repeatable method set forth in the specification.

Neither the instant record nor the prior art indicate the "CMRF-35" antibody is known and readily available to the public, and the antibody is not obtainable by a repeatable method set forth in the specification.

A deposit of the cell line(s) which produces the "CMRF-35" antibody may satisfy the enablement requirement of 35 USC 112, 1st paragraph. See 37 CFR 1.801-1.809 as well as MPEP § 2400.

For example, if a deposit of the antibody has already been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the cell line which produces the claimed antibody has been deposited under the Budapest Treaty and that the hybridoma *will be irrevocably and without restriction or condition released to the public upon the issuance of a patent* would satisfy the deposit requirement made herein. See 37 CFR 1.808.

Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer*. See 37 CFR 1.806.

If the antibody is deposited after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line that produces the claimed antibody(ies) described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

In conclusion, the instant claims encompass an invention of tremendous breadth, and essentially call for trial and error by the skilled artisan to begin discovering how to make and use the claimed invention without assisting the skilled artisan in such an endeavor, which is insufficient to constitute adequate enablement.

As put forth in Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), "[i]f mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Similarly, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 1001,(CAFC 1997), the court held: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". Further, "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

8. Claims 21-24, 29, 31, 32 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As set forth in Section 7 above, the instant claims recite (emphasis added), "A method…comprising obtaining a sample from said subject comprising T-cells ***and subjecting the sample to cell surface discrimination means to determine the presence, absence or level of CD4+ T-cells*** selected from the list consisting of CMRF-35++...CMRF-35+...CMRF-35-…"

While the claims do not recite "means for' or "step for" the phrase "subjecting the sample to cell surface discrimination means to determine the presence, absence or level of CD4+ T-cells" is sufficiently close so as to qualify as an invocation of 35 U.S.C. § 112, 6th paragraph. The instant specification discloses corresponding structure and acts for discriminating cell surface expression levels of the T-cell markers CD4 and CD45RO.

The instant specification also discloses CMRF-35++ CD45RO+ and more particularly, CMRF-35++ CD45RO+ CXCR3+ T-cells are absent from the peripheral blood of psoriasis patients as compared to normal controls, and exemplifies the discrimination of cell surface levels of "CMRF-35" with the "CMRF-35" antibody (see Section 7 above).

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Vas-Cath, Inc., v. Mahurkar, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116.

The issue here is does the instant specification provide adequate support for the genus of cell surface discrimination means to detect and distinguish CMRF-35++ from CMR-35+ and

CMRF-35-, and also to detect the same CMRF-35++ cells which applicant detected and characterized as decreased in disease, such as psoriasis as described in Section 7 above.

The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. In re Bell, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). In re Deuel, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995).

If the particular "CMRF-35" antibody described and exemplified in the instant specification were readily available then the instant specification would put the skilled artisan in possession of this particular species of means to detect CMRF-35 as part of the claimed invention.

However, this alone would not suffice to establish possession the genus of any means to detect CMRF-35 as claimed because applicant has not disclosed what particular epitope shared between CMRF-35A and CMRF-35H is recognized by the particular "CMRF-35" disclosed in the instant specification. Furthermore, isolating antibodies having affinity and specificity duplicating that of the particular "CMRF-35" disclosed in the instant specification in the absence of knowledge as to the particular epitope bound by the "CMRF-35" antibody is an unpredictable endeavor requiring far more than routine experimentation for the reasons given in Section 7 above.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function … does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/
Examiner, Art Unit 1644
December 17, 2008